Coherence analysis of brain activity associated with Tinnitus

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ABSTRACT

Tinnitus is ringing or buzzing or any sound perceived to be coming from the head or ears without an external sound source. Although no cure for tinnitus exists there are many treatments most of which provide only limited relief. The primary purpose of this study was to determine if MEG can detect cortical activity correlated with severity or location of tinnitus. Coherence is a measure of synchronization between brain regions. Synchronized activity within a neuronal network is determined by the strength of network connections. How well two or more brain regions are connected can be determined by measuring the coherence between these regions. We collected spontaneous MEG from patients with tinnitus and control subjects. All subjects wore ear plugs to eliminate outside sounds. Subjects kept their eyes open and fixated on point on the ceiling of the room. In these subjects MEG imaging showed highly coherent brain activity in the auditory cortex, contralateral to their perceived tinnitus. The control subjects had MEG coherence maps that displayed multiple brain areas active but no particular areas were found that were highly coherent. We determined that specific cortical areas in the auditory cortex, which may be responsible for tinnitus, are detectable using coherence mapping of the MEG signals. MEG can provide a technique that enables us to detect cortical neuronal activity that will be useful both in the diagnosis of tinnitus as well as the detection of improvements in the symptoms of tinnitus from different treatments.

KEYWORDS: Tinnitus, MEG, Coherence imaging

INTRODUCTION

Tinnitus is perceived as a ringing or buzzing sound coming from the head or ears without an external sound source [1, 2]. Tinnitus is a distressing symptom affecting up to 30% of the population (300 million world wide), with 2 to 4% severely debilitated [3]. Current conventional medical interventions fail to provide significant relief for most patients [3].

Several studies have shown that neural hyperactivity leads to the generation of tinnitus [4, 5]. The amplitude [5] and firing rate increases in the dorsal cochlear nucleus [6], inferior colliculus [7] and primary auditory cortex [8] after exposure to a sound at a level that causes neural response threshold shifts. Tinnitus is accompanied by a change of the tonotopic map in the auditory cortex [9]. There is a high positive association between subjective tinnitus strength and the amount of shift of the tinnitus frequency in the auditory cortex [9]. Tinnitus might hypothetically arise when auditory cortex cells are processing acoustic stimuli for which they are not genetically predestined, resulting in an auditory mismatch.

For many years it was thought that the buzzing or ringing sounds heard by people with tinnitus only originated in the ear, but functional imaging studies using PET have demonstrated that these phantom auditory sensations originate somewhere in brain, not in the ear [10]. Patients with chronic tinnitus underwent PET imaging which revealed 17 of 20 patients had increased activity in the primary auditory cortex on the left side while the other 3 patients had increased activity on the right side [10].

MEG, using a noise free environment, is better suited to detect functional activation arising from tinnitus than PET, or fMRI. MEG has been used to detect the tonotopic organization of the auditory cortex during complex sounds [11]. MEG has also been applied to the investigation of a limited number of tinnitus studies and has been used to detect differences in the auditory responses in tinnitus patients [12]. The time domain and the spectrotemporal patterns of the MEG frequency bands in patients with tinnitus were different from the non-tinnitus group of control subjects. Specifically, the m100 was larger and the m200 was absent or of low amplitude in patients with tinnitus. In addition, the m200 occurred significantly later in tinnitus as compared to control subjects. In a recent paper, we used MEG to localize the cortical areas that respond to the same pitch as the patient's tinnitus [2]. These areas were targeted for electrical stimulation to disrupt the tinnitus network. Another recent MEG study showed that there are frequency changes that take place in the brain after treatment using a neurofeedback approach [13].

METHODS

Two patients with unilateral tinnitus and 1 patient with bilateral tinnitus were recruited by Dr. Seidman. Five control subjects were also recruited for this study. Spontaneous MEG was collected while the subjects lay on the bed in the magnetically shielded room. MEG data were collected at 508Hz from 0.1-100 Hz then digitally filtered 1-50 Hz. All subjects wore ear plugs to eliminate outside sounds. Subjects kept their eyes open and fixated on a point on the ceiling of the room for the first 10 minute scan. Subjects then closed their eyes for the next 10 minute scan.

Data was frequency filtered 1-50Hz. Independent Component analysis was used to remove heart artifact from the MEG data and based on a singular valued decomposition (SVD) of MEG data some noise was eliminated [14]. MR-FOCUSS –ICA signal separation was applied to obtain signals from distinct cortical sources and MR-FOCUSS [15] was used to image cortical activation corresponding to these ICA signals. After imaging cortical activity, sources that interacted strongly with other sources were identified by calculating their average site-to-site coherence within each frequency band. Coherence calculations were based on transforming imaged source activity to a sequence of FFT spectra (256 time points with 25% overlap). Then, the cross-spectral matrix between active brain sources was calculated and normalized to obtain coherence magnitudes. Finally, for each active cortical site, the average coherence with all other sources was calculated for each frequency. Coherence images were generated for each consecutive 7.5 seconds of the 10 minutes of MEG data. These were averaged to obtain coherence magnitude and location of strongly interacting cortical sources. The variance across this set of images is a measure of the stability of the cortical network activity and allows changes in coherence across time to be assessed for statistical significance.

Coherence between cortical sites is a consequence of both direct and indirect connectivity within normal or abnormal cortical networks. These networks can be very transient or persistent as in the case of tinnitus. MEG coherence imaging is particularly effective for observing cortical sites involved in persistent network activity that dominates the duration of these 10 minute studies.

RESULTS

In subjects with tinnitus, highly coherent brain activity in the auditory cortex, contralateral to their perceived tinnitus dominated the coherence displays (Figures 1&2). The display threshold is 15% of the maximum coherence. In contrast, the scattered coherent regions, which were observed in the control subjects, did not include either auditory cortex and had lower average coherence magnitudes (not shown). Thus, we have demonstrated that specific cortical areas in the auditory cortex, which may be responsible for tinnitus, are detectable using coherence mapping of their MEG signals. Figure 1 displays the typical coherence images from a patient with unilateral tinnitus for a 10 minute scan with eyes open and ears plugged. We also investigated difference between eyes open and eyes closed. Highly coherent activity within the auditory cortex is clearly seen in both conditions (not shown). Also, we observed that regions of coherence, associated with alpha activity were increased in the eyes closed condition, as expected. Our third patient had bilateral tinnitus. His coherence images are shown in figure 2. Even though he stated that both ears were ringing, the calculated magnitude of coherent activity with in the region of the auditory cortex in the right hemisphere was greater than in the left hemisphere. These preliminary data show that MEG coherence imaging enables us to detect and quantify cortical neuronal activity for gauging the degree and severity of tinnitus. Thus, by utilizing MEG coherence imaging we will be able to establish an effective clinically diagnostic tool for the detection and evaluation of tinnitus.

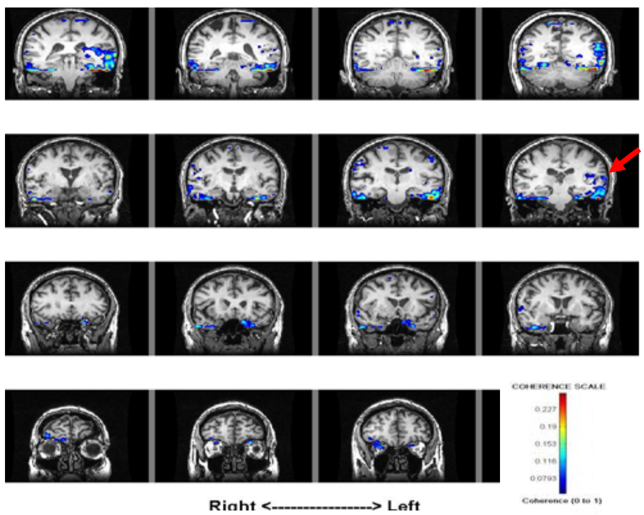

Fig 1. MEG Coherence analysis of spontaneous activity while patient perceived his tinnitus. MRI shows localization of activated cortex in the Left Auditory Cortex. Red indicates cortical areas that are highly coherent with all other brain regions. This patient had unilateral tinnitus in the right ear.

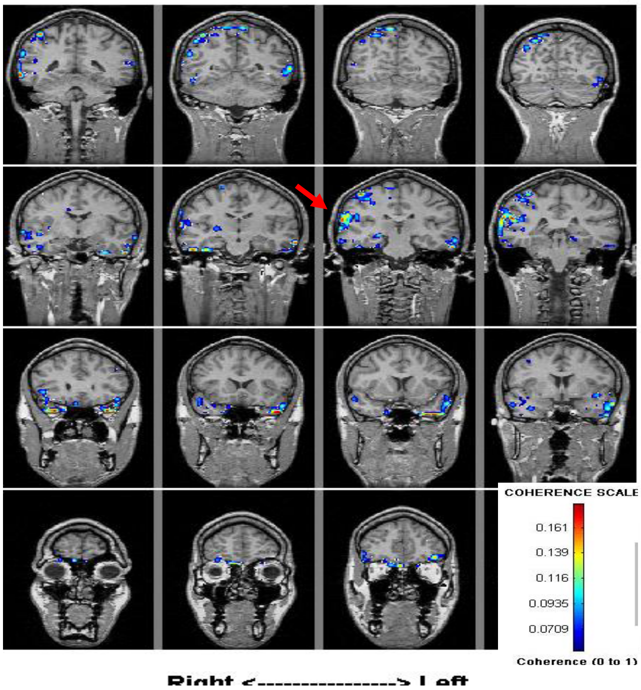

Fig 2. This patient has bilateral tinnitus. High coherence seen in the Right Auditory cortex even though he states both ears are ringing. This implies a network that is more interactive in the auditory cortex of the right hemisphere than in the left.

DISCUSSION

In this study we determined that the strength of cortical network interaction was correlated with tinnitus. MEG coherence images of network interactions from patients who have unilateral tinnitus localized to areas in temporal lobe of the hemisphere contralateral to the perceived sound. In the case of the patient who had bilateral tinnitus, the MEG scan found higher cortical coherence in one hemisphere. These results show that MEG can be used to detect brain activity from tinnitus.

CONCLUSION

This continuing research has the potential for establishing MEG neuroimaging as a clinical tool to determine specific brain circuitry related to tinnitus. MEG coherence imaging maybe used to provide clinicians with a diagnostic tool for assessing and evaluating tinnitus. By imaging the connectivity and coherence of the brain activity with MEG before and after treatment, we will gain understanding of the underlying brain mechanisms tinnitus. These studies may further the basic science of validating neuronal network models of auditory functioning. Accurate models of these neuronal networks may prove useful for the development of future tinnitus treatments.

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